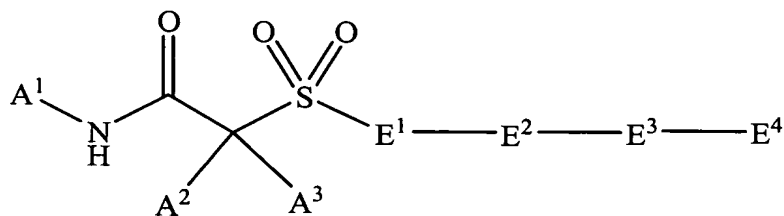


WE CLAIM:

1. A compound or a salt thereof, wherein:

the compound corresponds in structure to Formula 1-1:



(1-1); and

A¹ is selected from the group consisting of hydrogen, hydroxyl, carbocycloxy, and heterocycloxy; and

as to A² and A³:

A² and A³, together with the carbon to which they are both bonded, form heterocyclyl or carbocyclyl, wherein:

the heterocyclyl or carbocyclyl optionally is substituted with up to 3 independently selected R^x substituents, and

the heterocyclyl or carbocyclyl optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn,

optionally substituted with up to 3 independently selected R^x substituents, or

A² and A³ are independently selected from the group consisting of hydrogen, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocycloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylalkylthio, carbocyclylthioalkyl, carbocyclylalkylthioalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, heterocycloxyalkyl, heterocyclylalkoxyalkyl, heterocyclylalkylthio, heterocyclylthioalkyl, and heterocyclylalkylthioalkyl, wherein:

any member of such group optionally is substituted with up to 3
independently selected R^x substituents, and

any member of such group optionally is substituted with two
substituents such that the two substituents, together with the atom(s) to
5 which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the heterocyclyl and carbocyclyl optionally are

substituted with up to 3 independently selected R^x substituents;
and

E¹ is heteroaryl, wherein the heteroaryl optionally is substituted with one or
10 more independently selected R^x substituents; and

E² is carbocyclyl, wherein the carbocyclyl optionally is substituted with one or
more independently selected R^x substituents; and

E³ is selected from the group consisting of -O-, -C(O)-, -C(O)-O-, -O-C(O)-,
-N(R^b)-, -C(O)-N(R^b)-, -N(R^b)-C(O)-, -C(O)-N(R^b)-N(R^b)-C(O)-, -N(R^b)-C(O)-N(R^b)-,
15 -S-, -S(O)-, -S(O)₂-, -N(R^b)-S(O)₂-, -S(O)₂-N(R^b)-, -O-S(O)₂-, -S(O)₂-O-, -C(NH)-,
-C(NOH)-, -N(R^b)-C(NH)-, -N(R^b)-C(NOH)-, -C(NH)-N(R^b)-, -C(NOH)-N(R^b)-, alkyl,
alkenyl, carbonylalkyl, alkylcarbonyl, and a bond, wherein:

any alkyl or alkenyl portion of a substituent in such group optionally is
substituted with one or more independently selected R^c substituents; and

20 E⁴ is selected from the group consisting of hydrogen, halogen, cyano, alkyl,
alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylthioalkyl,
alkylthioalkylthioalkyl, alkylthioalkoxyalkyl, alkoxyalkylthioalkyl, aminoalkyl,
carbocyclyl, carbocyclylalkyl, carbocyclylalkoxyalkyl, heterocyclyl, heterocyclylalkyl,
and heterocyclylalkoxyalkyl, wherein:

25 any member of such group optionally is substituted with one or more
independently selected R^d substituents; and

each R^x is independently selected from the group consisting of halogen, cyano,
hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy,
R^b-oxyalkyl, alkenyloxy, alkynyloxy, alkylthio, R^bR^b-amino, R^bR^b-aminoalkyl,
30 R^bR^b-aminoalkoxy, R^bR^b-aminoalkyl(R^b)amino, carbocyclyl, carbocyclylalkyl,
carbocyclylloxy, carbocyclylloxyalkoxy, carbocyclylthio, heterocyclyl,

heterocyclalkyl, heterocycloxy, heterocycloxyalkoxy, heterocyclthio,
alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl,
alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclalkoxyalkyl,
carbocycliminocarbonyl, carbocyclthioalkyl, carbocyclsulfoxidoalkyl,
5 carbocyclsulfonylalkyl, carbocyclthioalkenyl, carbocyclsulfoxidoalkenyl,
carbocyclsulfonylalkenyl, heterocyclalkoxyalkyl, heterocyclthioalkyl,
heterocyclsulfoxidoalkyl, heterocyclsulfonylalkyl, heterocyclthioalkenyl,
heterocyclsulfoxidoalkenyl, heterocyclsulfonylalkenyl, heterocycliminocarbonyl,
aminosulfonylalkyl, and $-R^{x1}-R^{x2}$, wherein:

10 any member of such group optionally is substituted with one or more
substituents independently selected from the group consisting of halogen,
hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,
alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

any member of such group optionally is substituted with one or
15 more substituents independently selected from the group consisting of
halogen, hydroxy, and alkyl; and

each R^{x1} is selected from the group consisting of $-C(O)-$, $-C(S)-$, $-C(NR^y)-$,
 $-S(O)-$, and $-S(O)_2-$; and

each R^y is selected from the group consisting of hydrogen and hydroxy; and

20 each R^{x2} is selected from the group consisting of hydrogen, hydroxy, alkyl,
alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy, R^b -oxyalkyl, alkenyloxy,
alkynyloxy, R^bR^b -amino, R^bR^b -aminoalkyl, R^bR^b -aminoalkoxy,
 R^bR^b -aminoalkyl(R^b)amino, carbocycl, carbocyclalkyl, carbocycloxy,
carbocycloxyalkoxy, heterocycl, heterocyclalkyl, heterocycloxy, and
25 heterocycloxyalkoxy, wherein:

any member of such group optionally is substituted with one or more
substituents independently selected from the group consisting of halogen,
hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl,
alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy; and

each R^b is independently selected from the group consisting of hydrogen,
5 hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl, alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl, carbocyclylalkyl, carbocyclyloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl, carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocyclyloxyalkyl,
10 heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl, aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen,
15 hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkylcarbonyl, carbocyclyl, and carbocyclylalkyl; and

each R^c is independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, -C(H)(NH), -C(H)(NOH), thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, amino, alkyl, alkoxy, alkenyl, alkynyl, alkoxyalkyl, mono-alkylamino,
20 di-alkylamino, alkylthio, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,
25 aminocarbonyl, amino, alkyl, and carbocyclylalkyl; and

each R^d is independently selected from the group consisting of halogen, hydroxy, cyano, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, -N(R^e)₂, -C(O)(R^f), -S-R^e, -S(O)₂-R^e, carbocyclyl, alkylcarbocyclyl, alkoxy carbocyclyl, carbocyclylalkyl, heterocyclyl, alkylheterocyclyl, alkoxyheterocyclyl, and
30 heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen,

hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R^e is independently selected from the group consisting of hydrogen alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R^f is independently selected from the group consisting of hydrogen, alkyl, -O-R^e, -N(R^e)₂, carbocyclylalkyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino.

2. A compound or salt thereof according to claim 1, wherein A¹ is tetrahydropyranyloxy.

3. A compound or salt thereof according to claim 1, wherein A¹ is hydrogen.

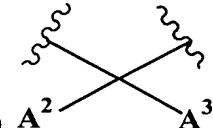
4. A compound or salt thereof according to claim 1, wherein A¹ is hydroxy.

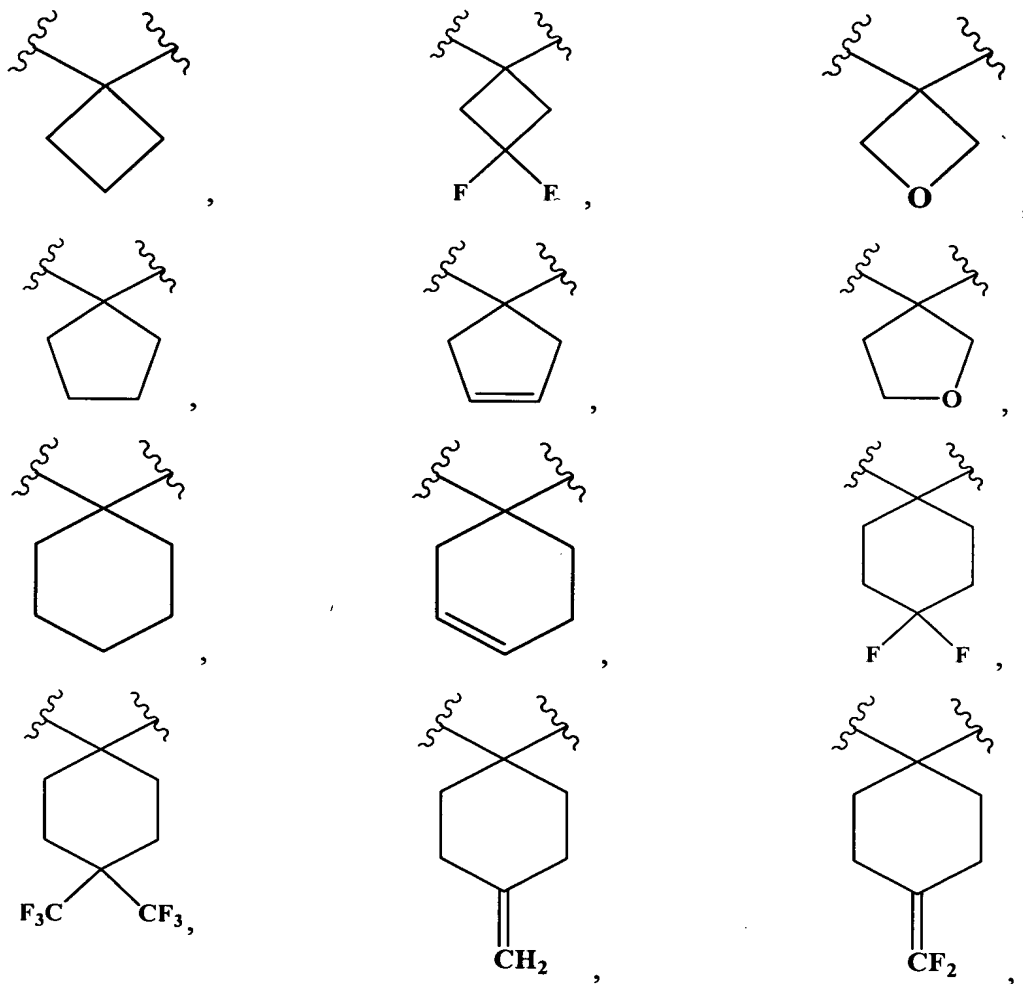
5. A compound or salt thereof according to claim 4, wherein A² and A³, together with the carbon to which they are both bonded, form heterocyclyl or carbocyclyl, wherein:

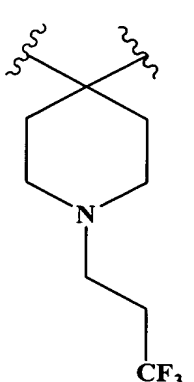
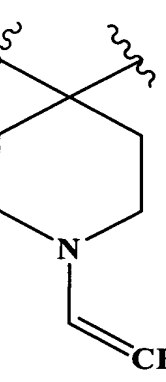
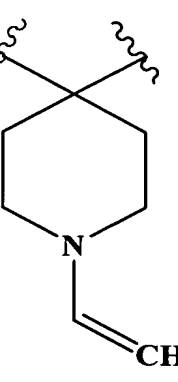
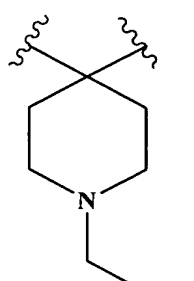
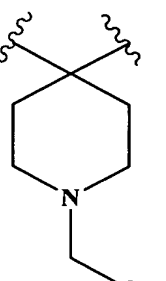
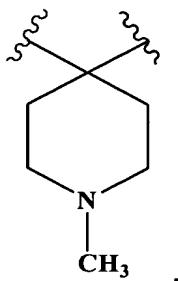
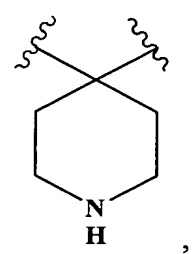
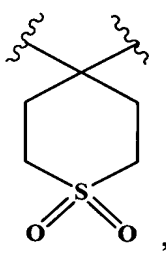
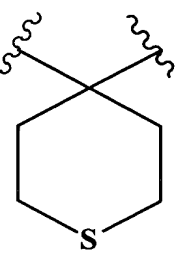
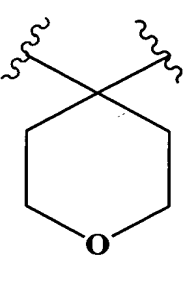
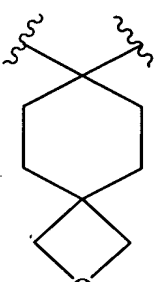
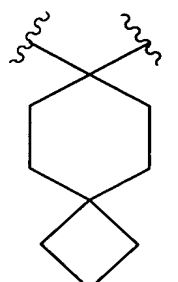
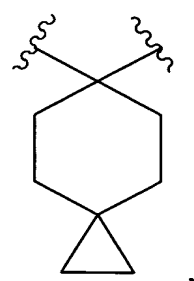
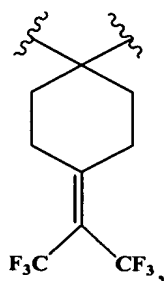
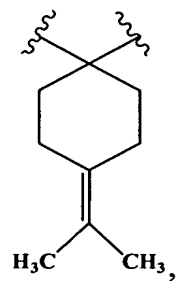
the heterocyclyl or carbocyclyl optionally is substituted with up to 3 independently selected R^x substituents, and

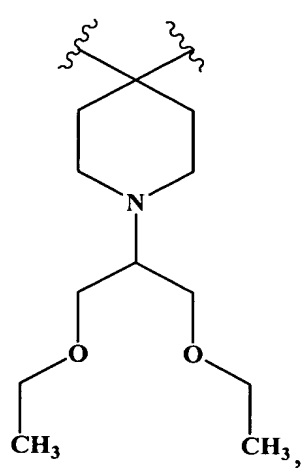
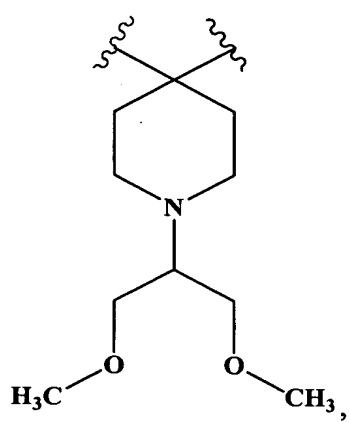
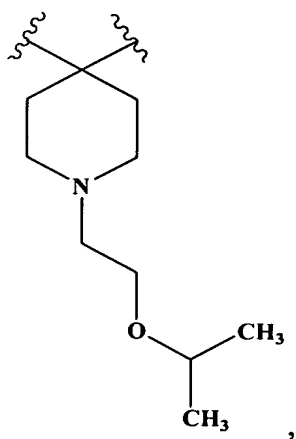
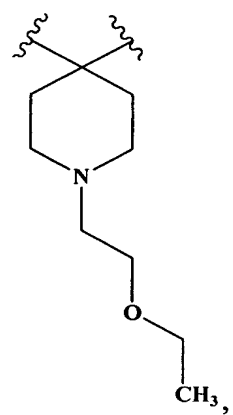
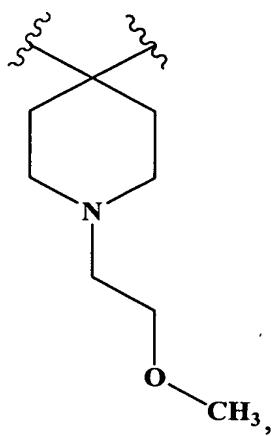
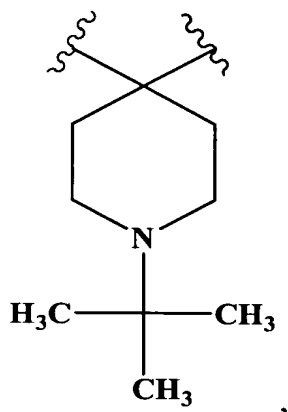
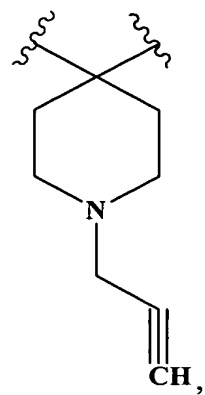
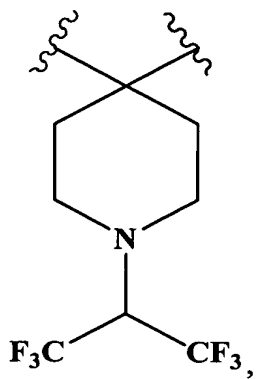
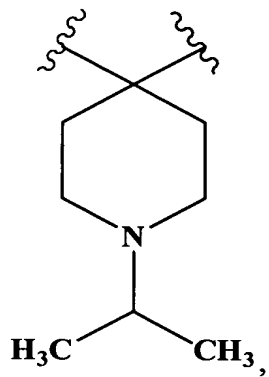
the heterocyclyl or carbocyclyl optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

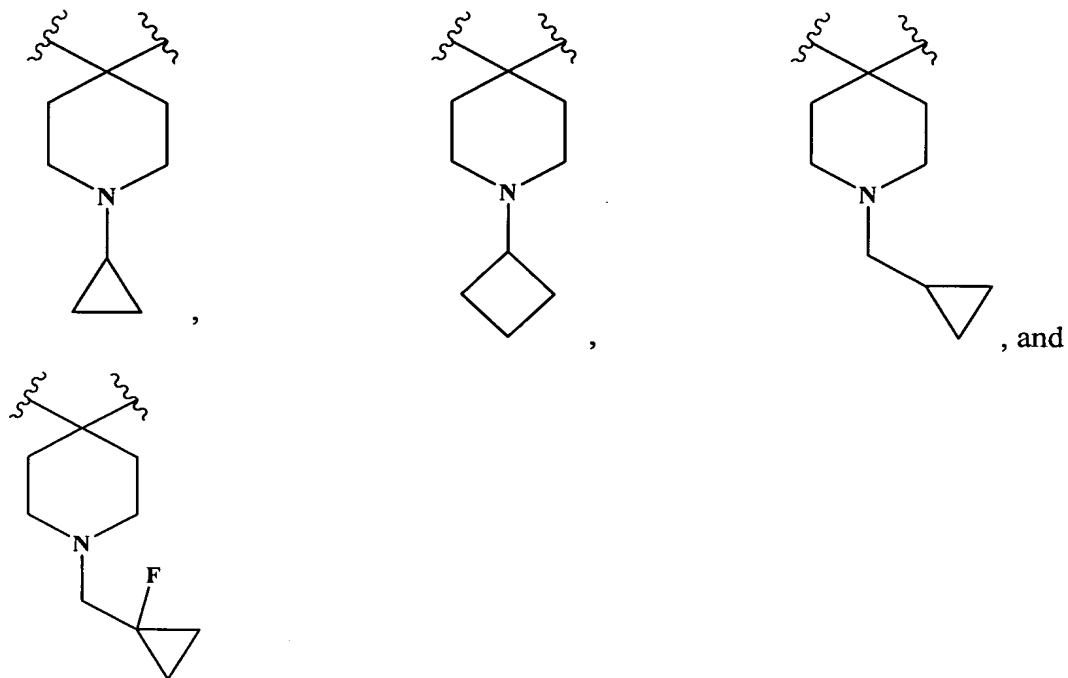
the optional heterocyclyl or carbocyclyl is, in turn, optionally substituted with up to 3 independently selected R^x substituents.

6. A compound or salt thereof according to claim 5, wherein A^2  A^3 is
5 selected from the group consisting of:

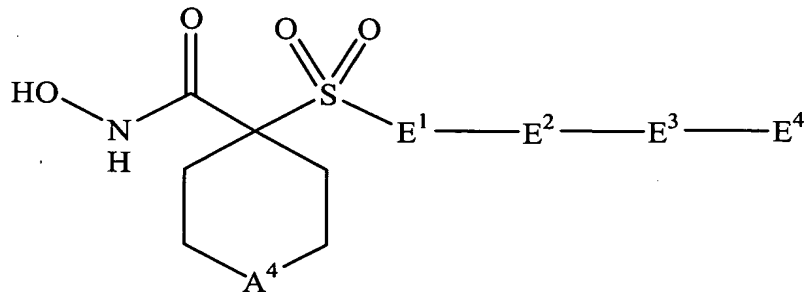






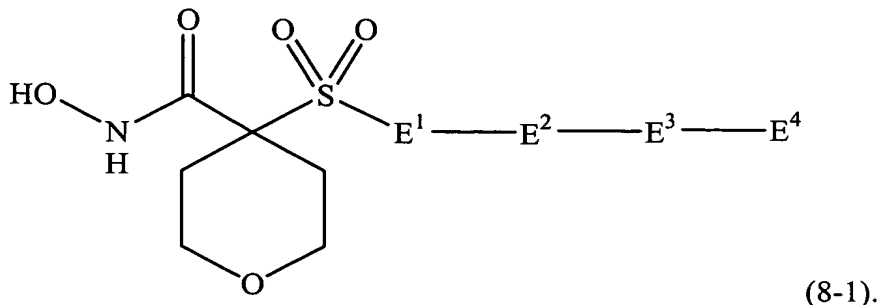


7. A compound or salt thereof according to claim 5, wherein:
the compound corresponds in structure to Formula (7-1):

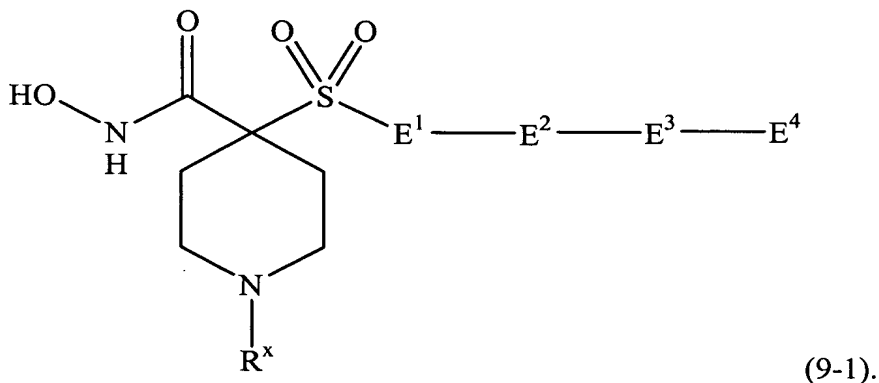


5 A^4 is selected from the group consisting of $-C(H)_2-$, $-C(R^x)(H)-$, $-C(R^x)_2-$, $-O-$, $-N(H)-$, $-N(R^x)-$, $-S-$, $-S(O)-$, and $-S(O)_2-$.

8. A compound or salt thereof according to claim 7, wherein the compound corresponds in structure to Formula (8-1):



9. A compound or salt thereof according to claim 7, wherein the compound corresponds in structure to Formula (9-1):



10. A compound or salt thereof according to claim 7, wherein E² is phenyl, wherein the phenyl optionally is substituted with one or more independently selected R^x substituents.

11. A compound or salt thereof according to claim 7, wherein E¹ is selected from the group consisting of furanyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiodiazolyl, oxadiazolyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, oxathiazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, oxathiazinyl, oxepinyl, thiepinyl, benzofuranyl, isobenzofuranyl, benzoxazolyl, benzoisoxazolyl, anthranilyl, benzothienyl, isobenzothienyl, benzothiazolyl, benzoisothiazolyl, benzothiadiazolyl, indoliziny, pyranopyrrolyl, benzoxadiazolyl, indolyl, isoindazolyl, benzoimidazolyl, benzotriazolyl, purinyl, imidazopyrazinyl,

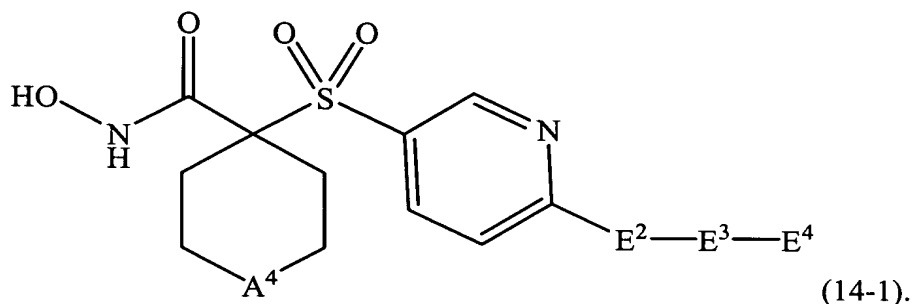
imidazolopyridazyl, quinolinyl, isoquinolinyl, pyridopyridinyl, phthalazinyl, quinoxalinyl, benzodiazinyl, pteridinyl, pyridazinotetrazinyl, pyrazinotetrazinyl, pyrimidinotetrazinyl, benzoimidazothiazolyl, carbazolyl, and acridinyl, wherein:

any member of such group optionally is substituted with one or more
independently selected R^x substituents.

12. A compound or salt thereof according to claim 11, wherein E¹ is a 5-member ring.

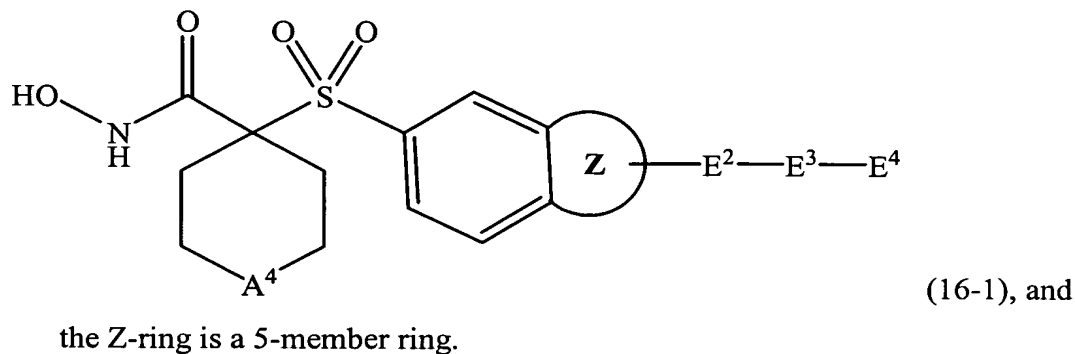
13. A compound or salt thereof according to claim 11, wherein E¹ is a 6-member ring.

14. A compound or salt thereof according to claim 13, wherein the compound corresponds in structure to Formula (14-1):



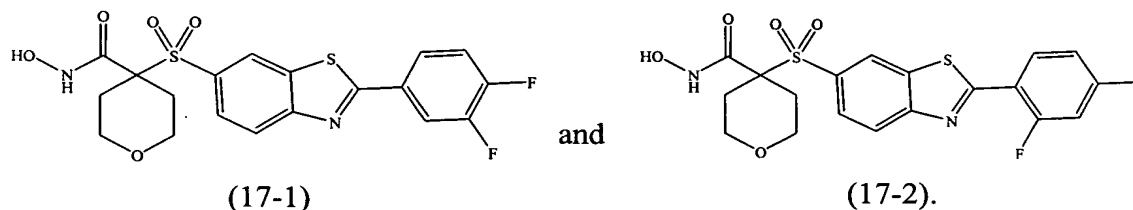
15. A compound or salt thereof according to claim 11, wherein E¹ is a 9-member fused-ring structure.

16. A compound or salt thereof according to claim 15, wherein:
the compound corresponds in structure to Formula (16-1):



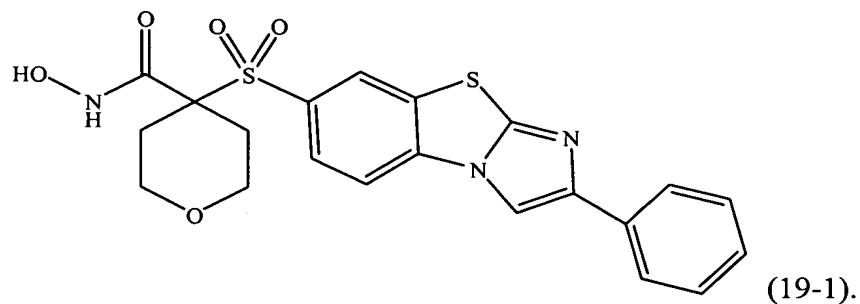
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17. A compound or salt thereof according to claim 16, wherein the compound
corresponds in structure to a formula selected from the group consisting of:



18. A compound or salt thereof according to claim 11, wherein E¹ is a
12-member fused-ring structure.

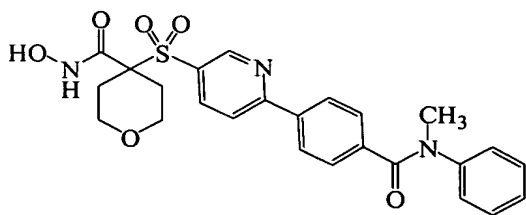
19. A compound or salt thereof according to claim 18, wherein the compound
corresponds in structure to Formula (19-1):



15

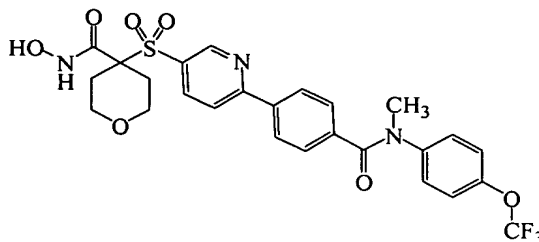
20. A compound or salt thereof according to claim 7, wherein E⁴ is carbocyclyl
optionally substituted with one or more independently selected R^d substituents.

21. A compound or salt thereof according to claim 20, wherein the compound corresponds in structure to a formula selected from the group consisting of:



(21-1)

and

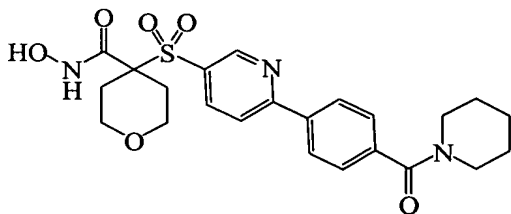


(21-2).

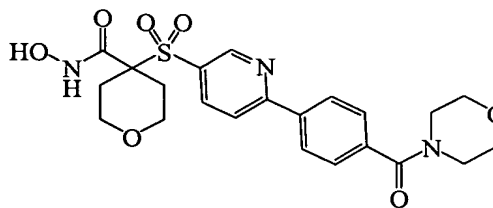
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22. A compound or salt thereof according to claim 7, wherein E⁴ is heterocyclyl optionally substituted with one or more independently selected R^d substituents.

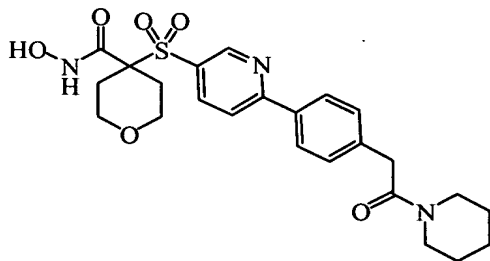
23. A compound or salt thereof according to claim 22, wherein the compound corresponds in structure to a formula selected from the group consisting of:



(23-1),



(23-2), and

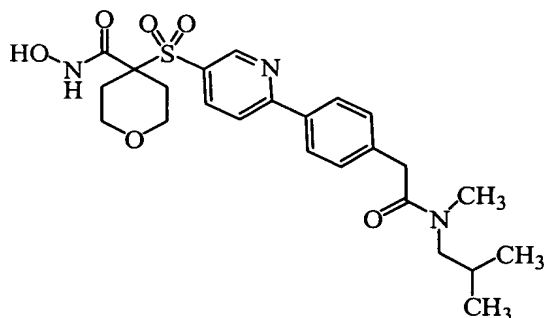


(23-3).

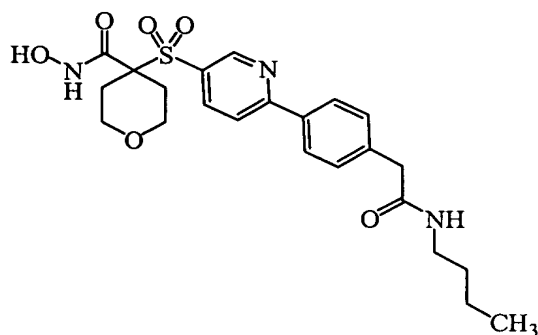
10

24. A compound or salt thereof according to claim 7, wherein E⁴ is aminoalkyl optionally substituted with one or more independently selected R^d substituents.

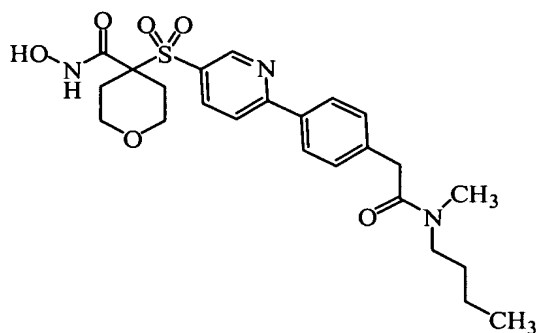
25. A compound or salt thereof according to claim 24, wherein the compound corresponds in structure to a formula selected from the group consisting of:



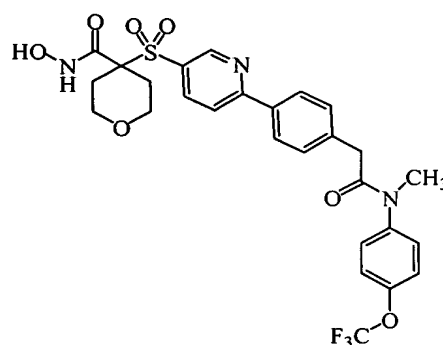
(25-1),



(25-2),



(25-3), and



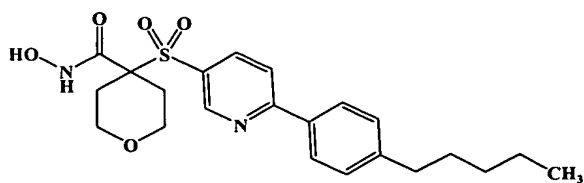
(25-4).

26. A compound or salt thereof according to claim 7, wherein E⁴ is selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl, alkylthioalkoxyalkyl, alkoxyalkylthioalkyl, and aminoalkyl, wherein:

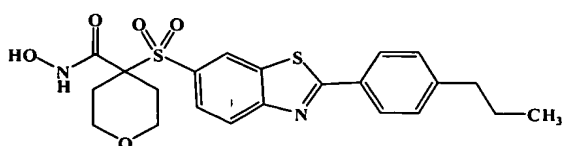
any member of such group optionally is substituted with one or more independently selected halogen.

27. A compound or salt thereof according to claim 26, wherein E³ is selected from the group consisting of a bond, -O-, -C(O)-N(H)-, -C(O)-N(CH₃)-, and -C(O)-N(CH₂CH₃)-.

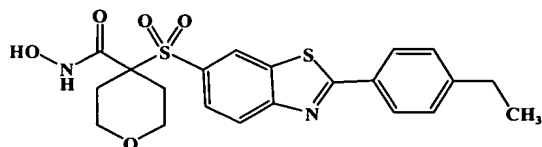
28. A compound or salt thereof according to claim 27, wherein the compound corresponds in structure to a formula selected from the group consisting of:



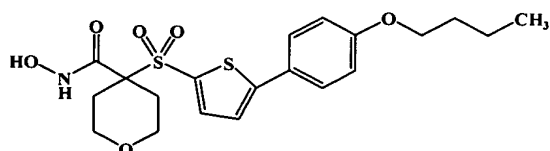
(28-1),



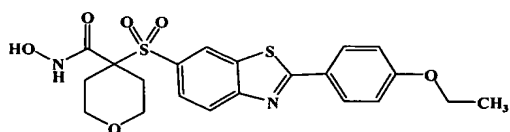
(28-2),



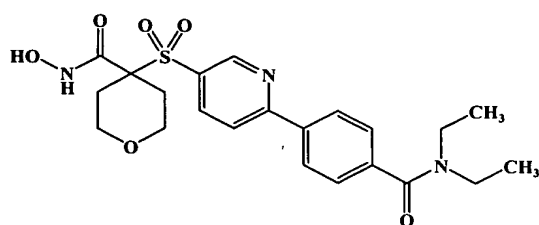
(28-3),



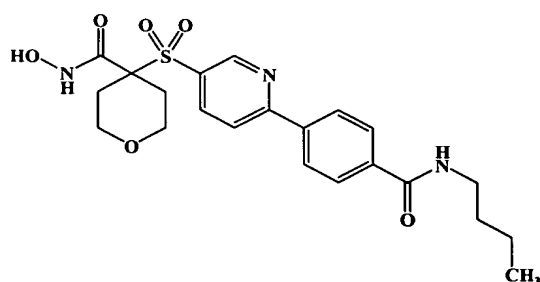
(28-4)



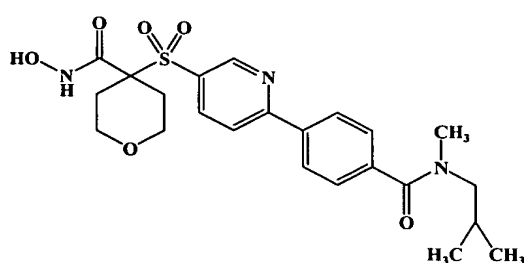
(28-5).



(28-6),



(28-7), and



(28-8).

29. A compound or salt thereof according to claim 26, wherein E⁴ is C₁-C₆-alkyl substituted with one or more fluoro.

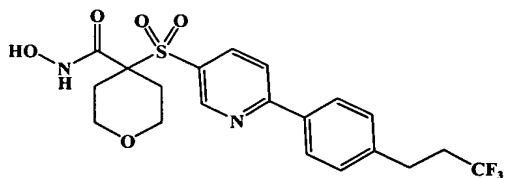
30. A compound or salt thereof according to claim 29, wherein E⁴ is selected from the group consisting of:

trifluoromethyl, and

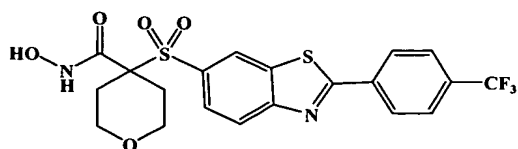
C₁-C₅-alkyl substituted with trifluoromethyl.

31. A compound or salt thereof according to claim 30, wherein E³ is selected from the group consisting of a bond, -O-, and -S-.

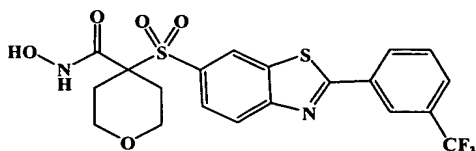
32. A compound or salt thereof according to claim 31, wherein the compound is selected from the group consisting of:



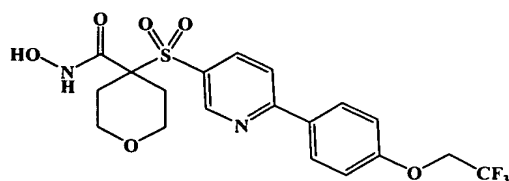
(32-1),



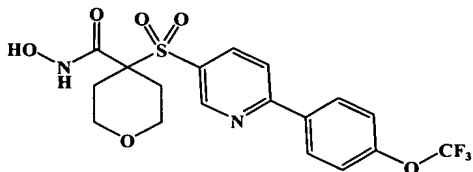
(32-2),



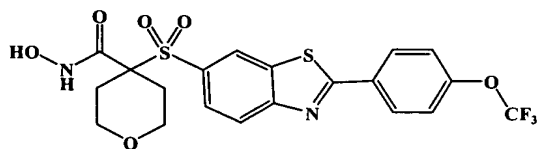
(32-3),



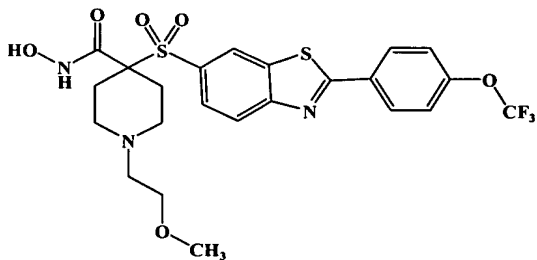
(32-4),



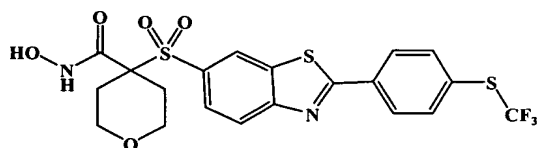
(32-5),



(32-6),



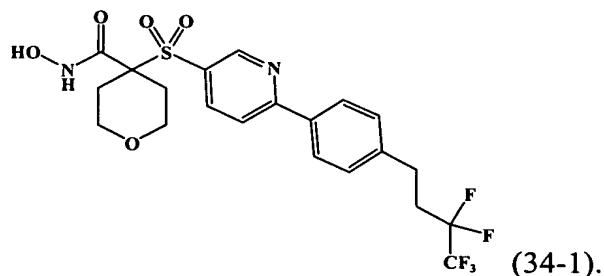
(32-7), and



(32-8).

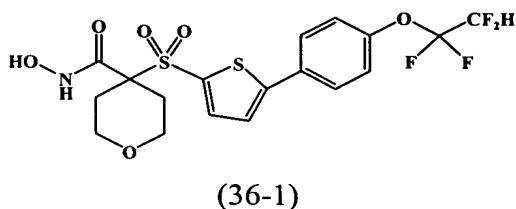
- 5 33. A compound or salt thereof according to claim 29, wherein E⁴ is selected from the group consisting of:
pentafluoroethyl, and
C₁-C₄-alkyl substituted with pentafluoroethyl.

34. A compound or salt thereof according to claim 33, wherein the compound corresponds in structure to Formula (34-1):

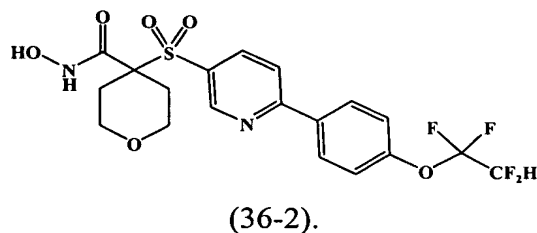


5 35. A compound or salt thereof according to claim 29, wherein E⁴ is C₁-C₆-alkyl comprising a carbon atom bonded to at least one hydrogen and at least one fluoro.

36. A compound or salt thereof according to claim 35, wherein the compound corresponds in structure to a formula selected from the group consisting of:

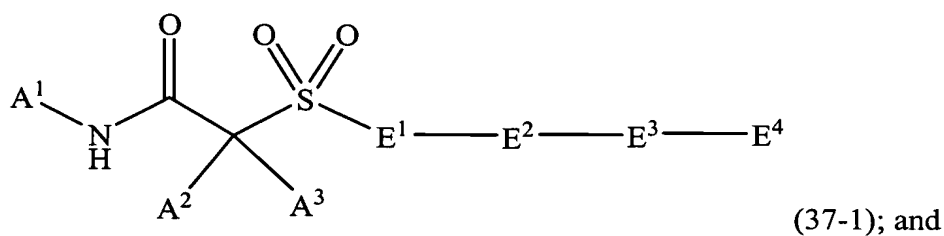


and



10

37. A compound or a salt thereof, wherein:
the compound corresponds in structure to Formula 37-1:



15 A¹ is selected from the group consisting of hydrogen, hydroxyl, carbocycloxy, and heterocycloxy; and

as to A² and A³:

A² and A³, together with the carbon to which they are both bonded, form heterocyclyl or carbocyclyl, wherein:

the heterocyclyl or carbocyclyl optionally is substituted with up to 3 independently selected R^x substituents, and

the heterocyclyl or carbocyclyl optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl substituent is, in turn, optionally substituted with up to 3 independently selected R^x substituents, or

A² and A³ are independently selected from the group consisting of hydrogen, alkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocyclyoxyalkyl, carbocyclylalkoxyalkyl, carbocyclylalkylthio, carbocyclylthioalkyl, carbocyclylalkylthioalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, heterocyclyoxyalkyl, heterocyclylalkoxyalkyl, heterocyclylalkylthio, heterocyclylthioalkyl, and heterocyclylalkylthioalkyl, wherein:

any member of such group optionally is substituted with up to 3 independently selected R^x substituents, and

any member of such group optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn, optionally substituted with up to 3 independently selected R^x substituents; and

E¹ is selected from the group consisting of furanyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiodiazolyl, oxadiazolyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, oxathiazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, oxathiazinyl, oxepinyl, thiepinyl, benzofuranyl, isobenzofuranyl, benzoxazolyl, benzoisoxazolyl, anthranilyl, benzothienyl, isobenzothienyl, benzothiazolyl, benzoisothiazolyl, benzothiadiazolyl, indoliziny, pyranopyrrolyl, benzoxadiazolyl, indolyl, isoindazolyl, benzoimidazolyl, benzotriazolyl, purinyl,

imidazopyrazinyl, imidazolopyridazyl, quinolinyl, isoquinolinyl, pyridopyridinyl, phthalazinyl, quinoxalinyl, benzodiazinyl, pteridinyl, pyridazinotetrazinyl, pyrazinotetrazinyl, pyrimidinotetrazinyl, benzoimidazothiazolyl, carbazolyl, and acridinyl, wherein:

5 any member of such group optionally is substituted with one or more independently selected R^x substituents; and

E² is heterocyclyl, wherein the heterocyclyl optionally is substituted with one or more independently selected R^x substituents; and

E³ is absent or selected from the group consisting of -O-, -C(O)-, -C(O)-O-,
10 -O-C(O)-, -N(R^b)-, -C(O)-N(R^b)-, -N(R^b)-C(O)-, -C(O)-N(R^b)-N(R^b)-C(O)-, -N(R^b)-C(O)-N(R^b)-, -S-, -S(O)-, -S(O)₂-, -N(R^b)-S(O)₂-, -S(O)₂-N(R^b)-, -O-S(O)₂-, -S(O)₂-O-, -C(NH)-, -C(NOH)-, -N(R^b)-C(NH)-, -N(R^b)-C(NOH)-, -C(NH)-N(R^b)-, -C(NOH)-N(R^b)-, alkyl, alkenyl, carbonylalkyl, alkylcarbonyl, and a bond, wherein:

15 any alkyl or alkenyl portion of a substituent in such group optionally is substituted with one or more independently selected R^c substituents; and

E⁴ is absent or selected from the group consisting of hydrogen, halogen, cyano, alkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl, alkylthioalkoxyalkyl, alkoxyalkylthioalkyl, aminoalkyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkoxyalkyl, heterocyclyl, heterocyclylalkyl,
20 and heterocyclylalkoxyalkyl, wherein:

any member of such group optionally is substituted with one or more independently selected R^d substituents; and

each R^x is independently selected from the group consisting of halogen, cyano, hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy, R^b-oxyalkyl, alkenyloxy, alkynyloxy, alkylthio, R^bR^b-amino, R^bR^b-aminoalkyl, R^bR^b-aminoalkoxy, R^bR^b-aminoalkyl(R^b)amino, carbocyclyl, carbocyclylalkyl, carbocyclylloxy, carbocyclylloxyalkoxy, carbocyclylthio, heterocyclyl, heterocyclylalkyl, heterocyclylloxy, heterocyclylloxyalkoxy, heterocyclylthio, alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl,
30 alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclylalkoxyalkyl, carbocyclyliminocarbonyl, carbocyclylthioalkyl, carbocyclylsulfoxidoalkyl,

carbocyclysulfonylalkyl, carbocyclylthioalkenyl, carbocyclysulfoxidoalkenyl,
carbocyclysulfonylalkenyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl,
heterocyclysulfoxidoalkyl, heterocyclysulfonylalkyl, heterocyclylthioalkenyl,
heterocyclysulfoxidoalkenyl, heterocyclysulfonylalkenyl, heterocyclyliminocarbonyl,
5 aminosulfonylalkyl, and $-R^{x1}-R^{x2}$, wherein:

any member of such group optionally is substituted with one or more
substituents independently selected from the group consisting of halogen,
hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,
alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

10 any member of such group optionally is substituted with one or
more substituents independently selected from the group consisting of
halogen, hydroxy, and alkyl; and

each R^{x1} is selected from the group consisting of $-C(O)-$, $-C(S)-$, $-C(NR^y)-$,
 $-S(O)-$, and $-S(O)_2-$; and

15 each R^y is selected from the group consisting of hydrogen and hydroxy; and

each R^{x2} is selected from the group consisting of hydrogen, hydroxy, alkyl,
alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy, R^b -oxyalkyl, alkenyloxy,
alkynyloxy, R^bR^b -amino, R^bR^b -aminoalkyl, R^bR^b -aminoalkoxy,
 R^bR^b -aminoalkyl(R^b)amino, carbocyclyl, carbocyclylalkyl, carbocyclyoxy,
20 carbocyclyoxyalkoxy, heterocyclyl, heterocyclylalkyl, heterocyclyoxy, and
heterocyclyoxyalkoxy, wherein:

any member of such group optionally is substituted with one or more
substituents independently selected from the group consisting of halogen,
hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl,
25 alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

any member of such group optionally is substituted with one or
more substituents independently selected from the group consisting of
halogen and hydroxy; and

each R^b is independently selected from the group consisting of hydrogen,
30 hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl,
alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl,

carbocyclylalkyl, carbocyclyloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl,
carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl,
carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocyclyloxyalkyl,
heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl,
5 heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl,
aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

any member of such group optionally is substituted with one or more
substituents independently selected from the group consisting of halogen,
hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl,
10 alkylcarbonyl, carbocyclyl, and carbocyclylalkyl; and

each R^c is independently selected from the group consisting of halogen,
hydroxy, cyano, carboxy, -C(H)(NH), -C(H)(NOH), thiol, sulfo, nitro, nitroso, oxo,
thioxo, imino, amino, alkyl, alkoxy, alkenyl, alkynyl, alkoxyalkyl, mono-alkylamino,
di-alkylamino, alkylthio, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, heterocyclyl,
15 and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more
substituents independently selected from the group consisting of halogen,
hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,
aminocarbonyl, amino, alkyl, and carbocyclylalkyl; and

20 each R^d is independently selected from the group consisting of halogen,
hydroxy, cyano, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl,
-N(R^e)₂, -C(O)(R^f), -S-R^e, -S(O)₂-R^e, carbocyclyl, alkylcarbocyclyl, alkoxycarbocyclyl,
carbocyclylalkyl, heterocyclyl, alkylheterocyclyl, alkylheterocyclyl, and
heterocyclylalkyl, wherein:

25 any member of such group optionally is substituted with one or more
substituents independently selected from the group consisting of halogen,
hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,
aminocarbonyl, and amino; and

each R^e is independently selected from the group consisting of hydrogen alkyl,
30 carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

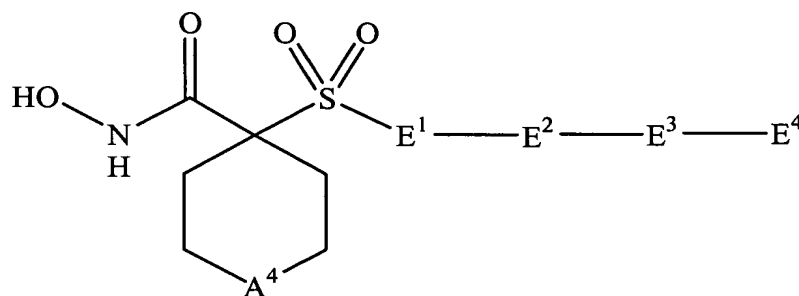
any member of such group optionally is substituted with one or more
substituents independently selected from the group consisting of halogen,

hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R^f is independently selected from the group consisting of hydrogen, alkyl, $-O-R^e$, $-N(R^e)_2$, carbocyclalkyl, and heterocyclalkyl, wherein:

5 any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino.

10 38. A compound or salt thereof according to claim 37, wherein:
the compound corresponds in structure to Formula (38-1):



(38-1); and

A^4 is selected from the group consisting of $C(H)_2-$, $-C(R^x)(H)-$, $-C(R^x)_2-$, $-O-$, $-N(H)-$, $-N(R^x)-$, $-S-$, $-S(O)-$, and $-S(O)_2-$.

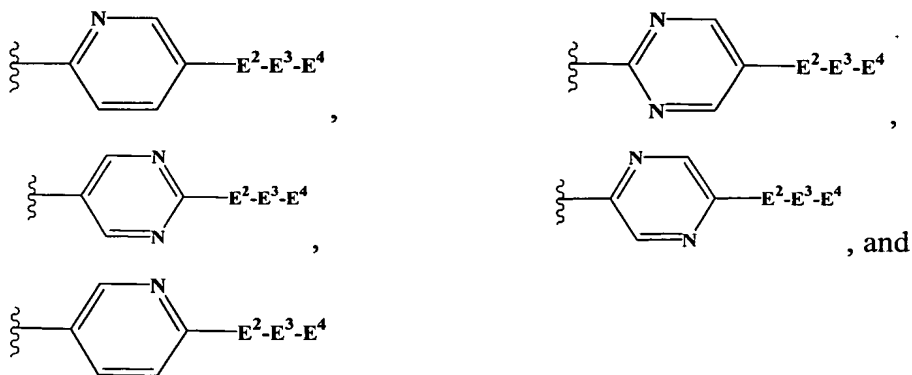
15 39. A compound or salt thereof according to claim 38, wherein E^1 is selected from the group consisting of oxazolyl, isoxazolyl, isothiazolyl, thiodiazolyl, oxadiazolyl, pyrrolyl, pyrazolyl, triazolyl, tetrazolyl, oxathiazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, oxathiazinyl, oxepinyl, thiepinyl, benzofuranyl, isobenzofuranyl, benzoisoxazolyl, anthranilyl, benzothienyl, isobenzothienyl, benzoisothiazolyl, benzothiadiazolyl, indolizinyl, pyranopyrrolyl, benzoxadiazolyl, indolyl, isoindazolyl, benzoimidazolyl, benzotriazolyl, purinyl, imidazopyrazinyl, imidazolopyridazyl, isoquinolinyl, pyridopyridinyl, phthalazinyl, quinoxalinyl, benzodiazinyl, pteridinyl, pyridazinotetrazinyl, pyrazinotetrazinyl, 20 pyrimidinotetrazinyl, benzoimidazothiazolyl, carbazolyl, and acridinyl, wherein:

any member of such group optionally is substituted with one or more independently selected R^x substituents.

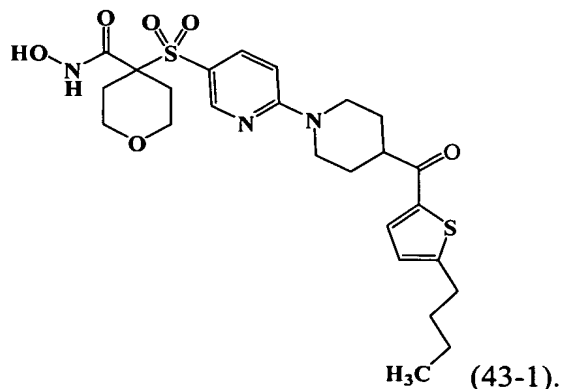
40. A compound or salt thereof according to claim 38, wherein E¹ is 5-member heteroaryl, wherein the heteroaryl optionally is substituted with one or more independently selected R^x substituents.

41. A compound or salt thereof according to claim 38, wherein E¹ is 6-member heteroaryl, wherein the heteroaryl optionally is substituted with one or more independently selected R^x substituents.

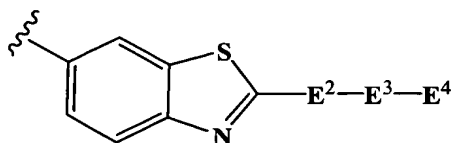
42. A compound or salt thereof according to claim 41, wherein -E¹-E²-E³-E⁴ corresponds in structure to a formula selected from the group consisting of:



43. A compound or salt thereof according to claim 42, wherein the compound corresponds in structure to Formula (43-1):

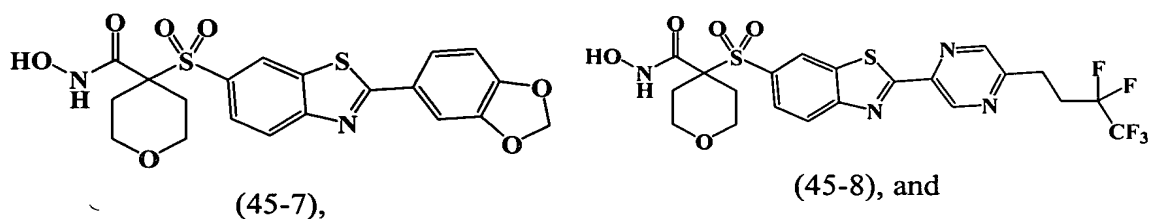
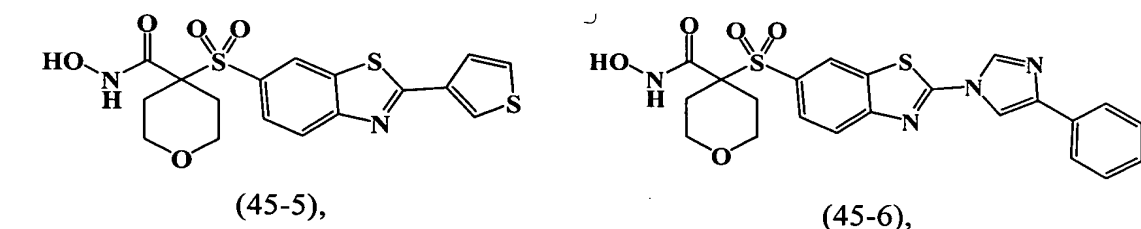
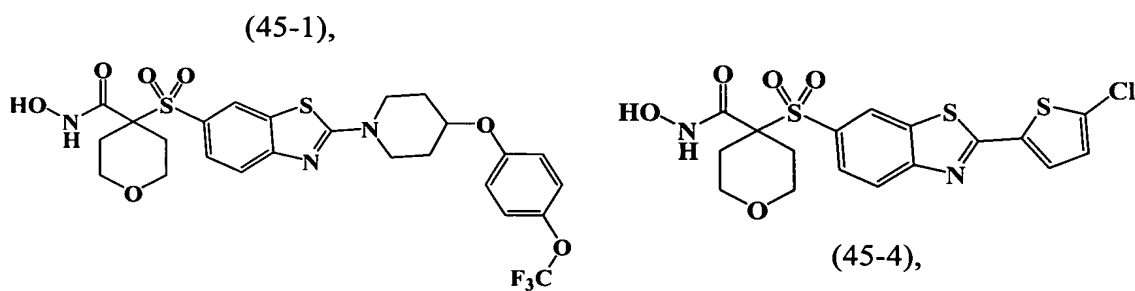
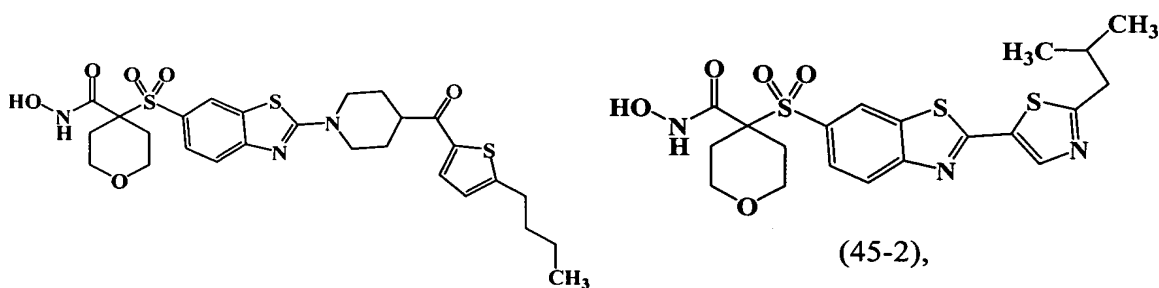


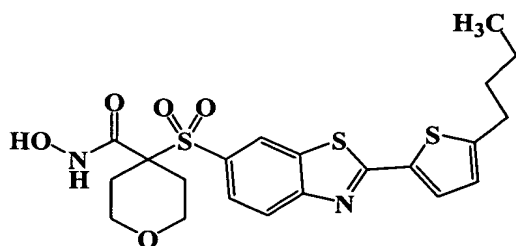
44. A compound or salt thereof according to claim 38, wherein $-E^1-E^2-E^3-E^4$ corresponds in structure to the following formula:



5

45. A compound or salt thereof according to claim 44, wherein the compound corresponds in structure to a formula selected from the group consisting of:



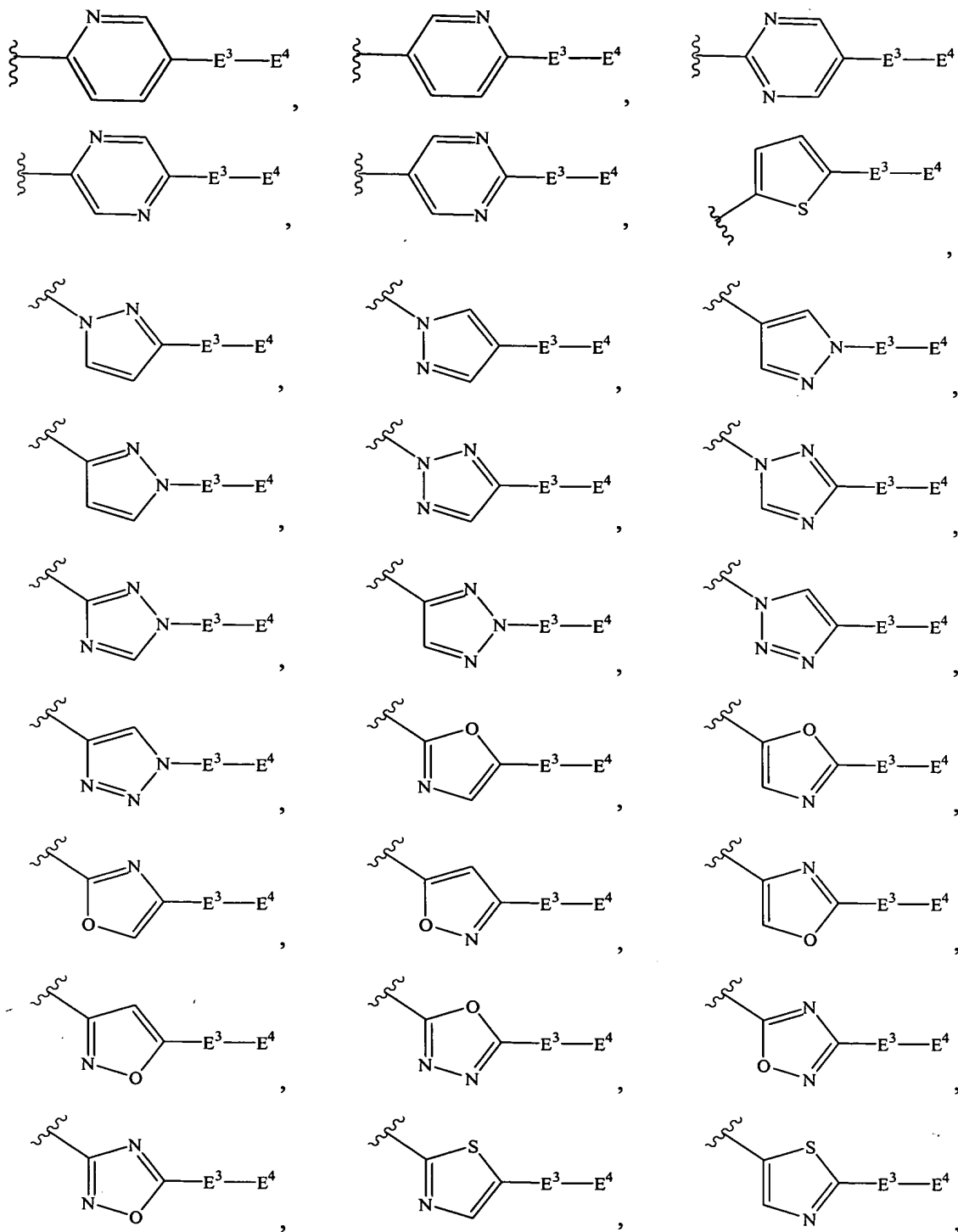


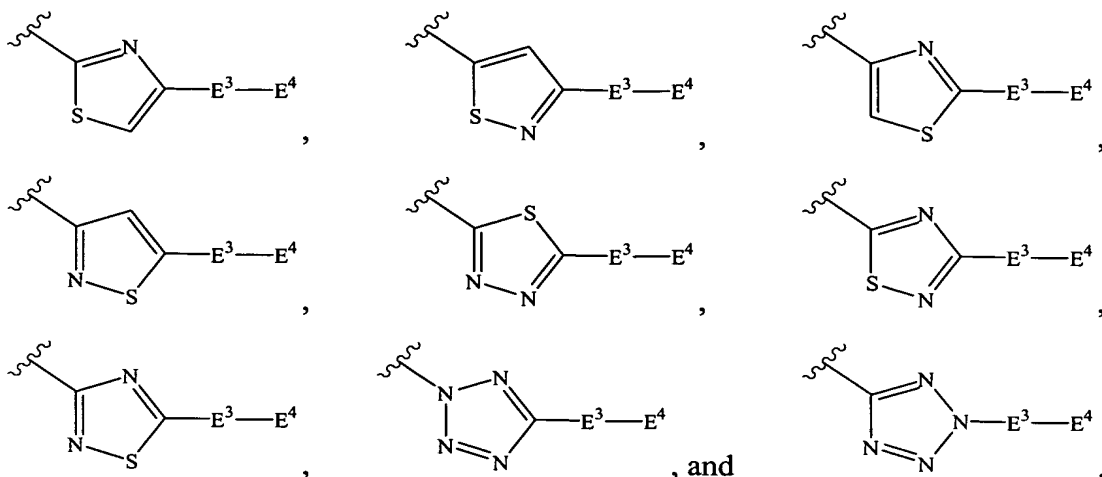
(45-9).

46. A compound or salt thereof according to claim 38, wherein E² is selected from the group consisting of furanyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiodiazolyl, oxadiazolyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, oxathiazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, oxathiazinyl, oxepinyl, thiepinyl, benzofuranyl, isobenzofuranyl, benzoxazolyl, benzoisoxazolyl, anthranilyl, benzothienyl, isobenzothienyl, benzothiazolyl, benzoisothiazolyl, benzothiadiazolyl, indoliziny, pyranopyrrolyl, benzoxadiazolyl, indolyl, isoindazolyl, benzoimidazolyl, benzotriazolyl, purinyl, imidazopyrazinyl, imidazolopyridazyl, quinolinyl, isoquinolinyl, pyridopyridinyl, phthalazinyl, quinoxaliny, benzodiazinyl, pteridinyl, pyridazinotetrazinyl, pyrazinotetrazinyl, pyrimidinotetrazinyl, benzoimidazothiazolyl, carbazolyl, acridinyl, oxatriazolyl, dihydrofuranyl, tetrahydrofuranyl, dihydrothienyl, tetrahydrothienyl, isopyrrolyl, pyrrolinyl, pyrrolidinyl, isoimidazolyl, imidazoliny, imidazolidinyl, pyrazoliny, pyrazolidinyl, dithiolyl, oxathiolyl, oxathiolanyl, oxazolidinyl, isoxazolidinyl, thiazoliny, isothiazoliny, thiazolidinyl, isothiazolidinyl, dioxazolyl, pyranyl, dihydropyranyl, tetrahydropyranyl, piperidinyl, piperazinyl, oxazinyl, isoxazinyl, oxadiazinyl, morpholinyl, azepinyl, diazepinyl, pyrindinyl, isoindolyl, indoleninyl, pyrazolopyrimidinyl, pyrazolopyrazinyl, pyrazolopyridazyl, benzodioxolyl, chromanyl, isochromanyl, thiochromanyl, isothiochromanyl, chromenyl, isochromenyl, thiochromenyl, isothiochromenyl, benzodioxanyl, tetrahydroisoquinolinyl, 4H-quinoliziny, benzoxazinyl, benzoisoxazinyl, benzoxadiazinyl, and xanthenyl, wherein:

any member of such group is optionally substituted with one or more independently selected R^x substituents.

47. A compound or salt thereof according to claim 46, wherein $-E^2-E^3-E^4$ is selected from the group consisting of:





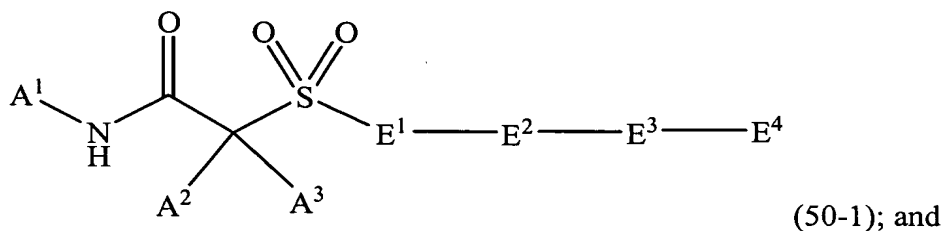
48. A compound or salt thereof according to claim 38, wherein E² is 5-member heterocyclyl, wherein the heterocyclyl optionally is substituted with one or more independently selected R^x substituents.

5

49. A compound or salt thereof according to claim 38, wherein E² is 6-member heterocyclyl, wherein the heterocyclyl optionally is substituted with one or more independently selected R^x substituents.

10

50. A compound or a salt thereof, wherein:
the compound corresponds in structure to Formula 50-1:



A¹ is selected from the group consisting of hydrogen, hydroxyl, carbocycloxy, and heterocycloxy; and

15

as to A² and A³:

A² and A³, together with the carbon to which they are both bonded, form heterocyclyl or carbocyclyl, wherein:

the heterocyclyl or carbocyclyl optionally is substituted with up to 3 independently selected R^x substituents, and

the heterocyclyl or carbocyclyl optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl substituent is, in turn, optionally substituted with up to 3 independently selected R^x substituents, or

A² and A³ are independently selected from the group consisting of hydrogen, alkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocyclyoxyalkyl, carbocyclylalkoxyalkyl, carbocyclylalkylthio, carbocyclylthioalkyl, carbocyclylalkylthioalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, heterocyclyoxyalkyl, heterocyclylalkoxyalkyl, heterocyclylalkylthio, heterocyclylthioalkyl, and heterocyclylalkylthioalkyl, wherein:

any member of such group optionally is substituted with up to 3 independently selected R^x substituents, and

any member of such group optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn, optionally substituted with up to 3 independently selected R^x substituents; and

E¹ is heteroaryl, wherein the heteroaryl optionally is substituted with one or more independently selected R^x substituents; and

E² is selected from the group consisting of carbocyclyl and heterocyclyl, wherein:

the carbocyclyl and heterocyclyl optionally are substituted with one or more independently selected R^x substituents; and

E³ is selected from the group consisting of -O-, -C(O)-, -C(O)-O-, -O-C(O)-, -N(R^b)-, -C(O)-N(R^b)-, -N(R^b)-C(O)-, -C(O)-N(R^b)-N(R^b)-C(O)-, -N(R^b)-C(O)-N(R^b)-, -S-, -S(O)-, -S(O)₂-, -N(R^b)-S(O)₂-, -S(O)₂-N(R^b)-, -O-S(O)₂-, -S(O)₂-O-, -C(NH)-, -C(NOH)-, -N(R^b)-C(NH)-, -N(R^b)-C(NOH)-, -C(NH)-N(R^b)-, -C(NOH)-N(R^b)-, alkyl,

5 alkenyl, carbonylalkyl, alkylcarbonyl, and a bond, wherein:

any alkyl or alkenyl portion of a substituent in such group optionally is substituted with one or more independently selected R^c substituents; and

E⁴ is selected from the group consisting of halogen, cyano, alkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl, 10 alkylthioalkoxyalkyl, alkoxyalkylthioalkyl, aminoalkyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkoxyalkyl, heterocyclyl, heterocyclylalkyl, and heterocyclylalkoxyalkyl, wherein:

any member of such group optionally is substituted with one or more independently selected R^d substituents; and

15 each R^x is independently selected from the group consisting of halogen, cyano, hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy, R^b-oxyalkyl, alkenyloxy, alkynyloxy, alkylthio, R^bR^b-amino, R^bR^b-aminoalkyl, R^bR^b-aminoalkoxy, R^bR^b-aminoalkyl(R^b)amino, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, carbocyclyloxyalkoxy, carbocyclylthio, heterocyclyl, 20 heterocyclylalkyl, heterocyclyloxy, heterocyclyloxyalkoxy, heterocyclylthio, alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl, alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclylalkoxyalkyl, carbocyclyliminocarbonyl, carbocyclylthioalkyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonylalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkenyl, 25 carbocyclylsulfonylalkenyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonylalkyl, heterocyclylthioalkenyl, heterocyclylsulfoxidoalkenyl, heterocyclylsulfonylalkenyl, heterocyclyliminocarbonyl, aminosulfonylalkyl, and -R^{x1}-R^{x2}, wherein:

any member of such group optionally is substituted with one or more 30 substituents independently selected from the group consisting of halogen,

hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and alkyl; and

each R^{x1} is selected from the group consisting of -C(O)-, -C(S)-, -C(NR^y)-, -S(O)-, and -S(O)₂-; and

each R^y is selected from the group consisting of hydrogen and hydroxy; and

each R^{x2} is selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy, R^b-oxyalkyl, alkenyloxy, alkynyloxy, R^bR^b-amino, R^bR^b-aminoalkyl, R^bR^b-aminoalkoxy, R^bR^b-aminoalkyl(R^b)amino, carbocyclyl, carbocyclylalkyl, carbocyclyoxy, carbocyclyoxyalkoxy, heterocyclyl, heterocyclylalkyl, heterocyclyoxy, and heterocyclyoxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy; and

each R^b is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl, alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl, carbocyclylalkyl, carbocyclyoxyalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl, carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocyclyoxyalkyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl, aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkylcarbonyl, carbocyclyl, and carbocyclylalkyl; and

5 each R^c is independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, -C(H)(NH), -C(H)(NOH), thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, amino, alkyl, alkoxy, alkenyl, alkynyl, alkoxyalkyl, mono-alkylamino, di-alkylamino, alkylthio, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkyl, wherein:

10 any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, amino, alkyl, and carbocyclylalkyl; and

15 each R^d is independently selected from the group consisting of halogen, hydroxy, cyano, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, -N(R^e)₂, -C(O)(R^f), -S-R^e, -S(O)₂-R^e, carbocyclyl, alkylcarbocyclyl, alkylcarbocyclyl, carbocyclylalkyl, heterocyclyl, alkylheterocyclyl, alkoxyheterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

20 each R^e is independently selected from the group consisting of hydrogen alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

25 any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

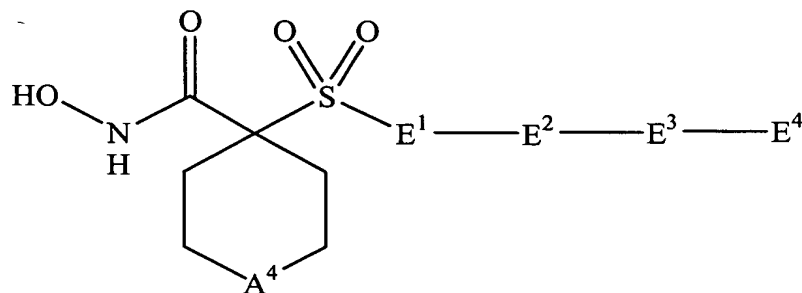
30 each R^f is independently selected from the group consisting of hydrogen, alkyl, -O-R^e, -N(R^e)₂, carbocyclylalkyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen,

hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino.

51. A compound or salt thereof according to claim 50, wherein E¹ is selected from the group consisting of furanyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiodiazolyl, oxadiazolyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, oxathiazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, oxathiazinyl, oxepinyl, thiepinyl, benzofuranyl, isobenzofuranyl, benzoxazolyl, benzoisoxazolyl, anthranilyl, benzothienyl, isobenzothienyl, benzothiazolyl, benzoisothiazolyl, benzothiadiazolyl, indoliziny, pyranopyrrolyl, benzoxadiazolyl, indolyl, isoindazolyl, benzoimidazolyl, benzotriazolyl, purinyl, imidazopyrazinyl, imidazolopyridazyl, quinolinyl, isoquinolinyl, pyridopyridinyl, phthalazinyl, quinoxalinyl, benzodiazinyl, pteridinyl, pyridazinotetrazinyl, pyrazinotetrazinyl, pyrimidinotetrazinyl, benzoimidazothiazolyl, carbazolyl, and acridinyl, wherein:
any member of such group optionally is substituted with one or more independently selected R^x substituents.

52. A compound or salt thereof according to claim 50, wherein:
the compound corresponds in structure to Formula (52-1):



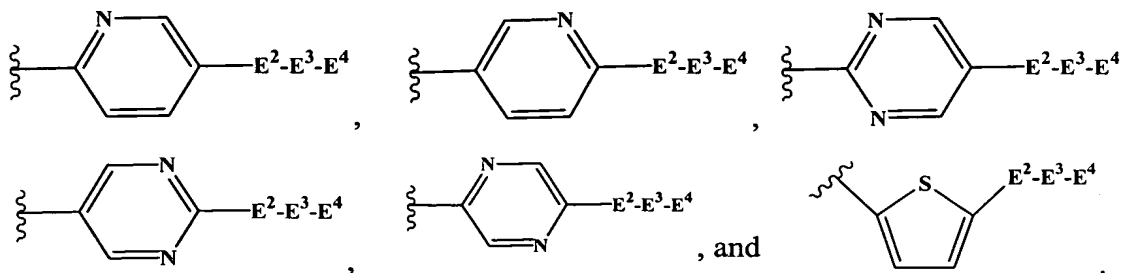
A⁴ is selected from the group consisting of -C(H)₂-, -C(R^x)(H)-, -C(R^x)₂-, -O-, -N(H)-, -N(R^x)-, -S-, -S(O)-, and -S(O)₂-.

53. A compound or salt thereof according to claim 52, wherein E² is selected from the group consisting of furanyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiodiazolyl, oxadiazolyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl,

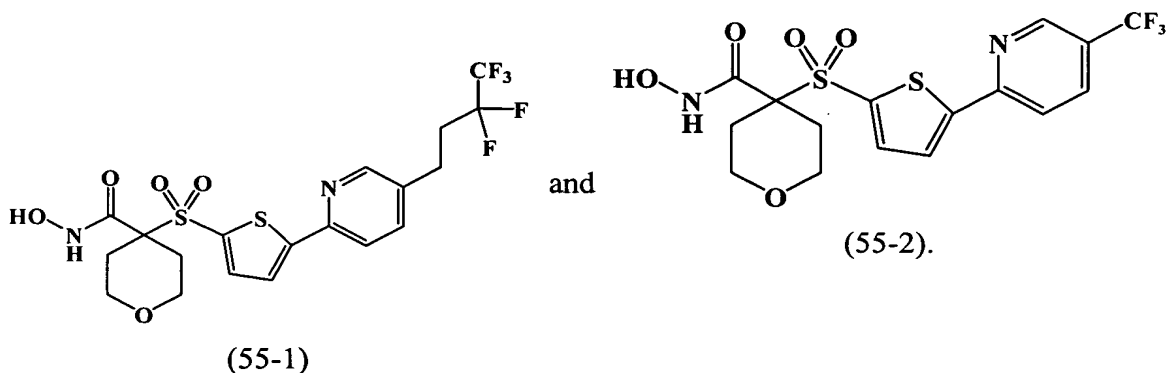
tetrazolyl, oxathiazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl,
oxathiazinyl, oxepinyl, thiepinyl, benzofuranyl, isobenzofuranyl, benzoxazolyl,
benzoxisoxazolyl, anthranilyl, benzothienyl, isobenzothienyl, benzothiazolyl,
benzoxisothiazolyl, benzothiadiazolyl, indolizinyl, pyranopyrrolyl, benzoxadiazolyl,
5 indolyl, isoindazolyl, benzoimidazolyl, benzotriazolyl, purinyl, imidazopyrazinyl,
imidazolopyridazyl, quinolinyl, isoquinolinyl, pyridopyridinyl, phthalazinyl,
quinoxalinyl, benzodiazinyl, pteridinyl, pyridazinotetrazinyl, pyrazinotetrazinyl,
pyrimidinotetrazinyl, benzoimidazothiazolyl, carbazolyl, acridinyl, dihydrofuranyl,
tetrahydrofuranyl, dihydrothienyl, tetrahydrothienyl, isopyrrolyl, pyrrolinyl,
10 pyrrolidinyl, isoimidazolyl, imidazolyl, imidazolidinyl, pyrazolinyl, pyrazolidinyl,
dithiolyl, oxathiolyl, oxathiolanyl, oxazolidinyl, isoxazolidinyl, thiazolinyl,
isothiazolinyl, thiazolidinyl, isothiazolidinyl, dioxazolyl, pyranyl, dihydropyranyl,
tetrahydropyranyl, piperidinyl, piperazinyl, oxazinyl, isoxazinyl, oxadiazinyl,
morpholinyl, azepinyl, diazepinyl, pyrindinyl, isoindolyl, indoleninyl,
15 pyrazolopyrimidinyl, pyrazolopyrazinyl, pyrazolopyridazyl, benzodioxolyl, chromanyl,
isochromanyl, thiochromanyl, isothiochromanyl, chromenyl, isochromenyl,
thiochromenyl, isothiochromenyl, benzodioxanyl, tetrahydroisoquinolinyl,
4H-quinolizinyl, benzoxazinyl, benzoisoxazinyl, benzoxadiazinyl, and xanthenyl,
wherein:

20 any member of such group optionally is substituted with one or more
independently selected R^x substituents.

54. A compound or salt thereof according to claim 53, wherein -E¹-E²-E³-E⁴
corresponds in structure to a formula selected from the group consisting of:



55. A compound or salt thereof according to claim 54, wherein the compound corresponds in structure to a formula selected from the group consisting of:



56. A method for treating a condition associated with pathologically excessive matrix metalloprotease, TNF- α convertase, or aggrecanase activity in a mammal, wherein the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 1 to the mammal in an amount that is therapeutically effective to treat the condition.

57. A method according to claim 56, wherein A¹ is hydrogen.

58. A method according to claim 56, wherein A¹ is hydroxy.

59. A method for treating a pathological condition in a mammal, wherein:
the pathological condition is selected from the group consisting of tissue destruction, a fibrotic disease, matrix weakening, defective injury repair, a cardiovascular disease, a pulmonary disease, a kidney disease, a liver disease, an ophthalmologic disease, and a central nervous system disease; and
the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 1 to the mammal in an amount that is therapeutically effective to treat the pathological condition.

60. A method for treating a pathological condition in a mammal, wherein:
the pathological condition is selected from the group consisting of osteoarthritis, rheumatoid arthritis, septic arthritis, tumor invasion, tumor metastasis, tumor angiogenesis, a decubitus ulcer, a gastric ulcer, a corneal ulcer, periodontal disease,
5 liver cirrhosis, fibrotic lung disease, otosclerosis, atherosclerosis, multiple sclerosis, dilated cardiomyopathy, epidermal ulceration, epidermolysis bullosa, aortic aneurysm, defective injury repair, an adhesion, scarring, congestive heart failure, post myocardial infarction, coronary thrombosis, emphysema, proteinuria, Alzheimer's disease, bone disease, chronic obstructive pulmonary disease, and a disease of the central nervous
10 system; and

the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 1 to the mammal in an amount that is therapeutically effective to treat the pathological condition.

15 61. A method for treating a pathological condition of the central nervous system in a mammal, wherein the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 1 to the mammal in an amount that is therapeutically effective to treat the pathological condition.

20 62. A pharmaceutical composition, wherein the composition comprises a therapeutically-effective amount of a compound (or a pharmaceutically acceptable salt thereof) recited in claim 1.

25 63. A method for treating a condition associated with pathologically excessive matrix metalloprotease, TNF- α convertase, or aggrecanase activity in a mammal, wherein the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 37 to the mammal in an amount that is therapeutically effective to treat the condition.

30 64. A method according to claim 63, wherein A¹ is hydrogen.

65. A method according to claim 63, wherein A¹ is hydroxy.

66. A method for treating a pathological condition in a mammal, wherein:
the pathological condition is selected from the group consisting of tissue
destruction, a fibrotic disease, matrix weakening, defective injury repair, a
5 cardiovascular disease, a pulmonary disease, a kidney disease, a liver disease, an
ophthalmologic disease, and a central nervous system disease; and
the method comprises administering a compound (or a pharmaceutically
acceptable salt thereof) recited in claim 37 to the mammal in an amount that is
therapeutically effective to treat the pathological condition.

10 67. A method for treating a pathological condition in a mammal, wherein:
the pathological condition is selected from the group consisting of osteoarthritis,
rheumatoid arthritis, septic arthritis, tumor invasion, tumor metastasis, tumor
angiogenesis, a decubitis ulcer, a gastric ulcer, a corneal ulcer, periodontal disease,
15 liver cirrhosis, fibrotic lung disease, otosclerosis, atherosclerosis, multiple sclerosis,
dilated cardiomyopathy, epidermal ulceration, epidermolysis bullosa, aortic aneurysm,
defective injury repair, an adhesion, scarring, congestive heart failure, post myocardial
infarction, coronary thrombosis, emphysema, proteinuria, Alzheimer's disease, bone
disease, chronic obstructive pulmonary disease, and a disease of the central nervous
20 system; and

the method comprises administering a compound (or a pharmaceutically
acceptable salt thereof) recited in claim 37 to the mammal in an amount that is
therapeutically effective to treat the pathological condition.

25 68. A method for treating a pathological condition of the central nervous system
in a mammal, wherein the method comprises administering a compound (or a
pharmaceutically acceptable salt thereof) recited in claim 37 to the mammal in an
amount that is therapeutically effective to treat the pathological condition.

30 69. A pharmaceutical composition, wherein the composition comprises a
therapeutically-effective amount of a compound (or a pharmaceutically acceptable salt
thereof) recited in claim 37.

70. A method for treating a condition associated with pathologically excessive matrix metalloprotease, TNF- α convertase, or aggrecanase activity in a mammal, wherein the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 50 to the mammal in an amount that is therapeutically effective to treat the condition.

71. A method according to claim 70, wherein A¹ is hydrogen.

72. A method according to claim 70, wherein A¹ is hydroxy.

73. A method for treating a pathological condition in a mammal, wherein: the pathological condition is selected from the group consisting of tissue destruction, a fibrotic disease, matrix weakening, defective injury repair, a cardiovascular disease, a pulmonary disease, a kidney disease, a liver disease, an ophthalmologic disease, and a central nervous system disease; and the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 50 to the mammal in an amount that is therapeutically effective to treat the pathological condition.

74. A method for treating a pathological condition in a mammal, wherein: the pathological condition is selected from the group consisting of osteoarthritis, rheumatoid arthritis, septic arthritis, tumor invasion, tumor metastasis, tumor angiogenesis, a decubitis ulcer, a gastric ulcer, a corneal ulcer, periodontal disease, liver cirrhosis, fibrotic lung disease, otosclerosis, atherosclerosis, multiple sclerosis, dilated cardiomyopathy, epidermal ulceration, epidermolysis bullosa, aortic aneurysm, defective injury repair, an adhesion, scarring, congestive heart failure, post myocardial infarction, coronary thrombosis, emphysema, proteinuria, Alzheimer's disease, bone disease, chronic obstructive pulmonary disease, and a disease of the central nervous system; and

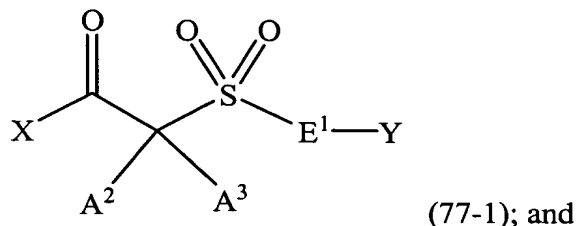
the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 50 to the mammal in an amount that is therapeutically effective to treat the pathological condition.

75. A method for treating a pathological condition of the central nervous system in a mammal, wherein the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 50 to the mammal in an amount that is therapeutically effective to treat the pathological condition.

76. A pharmaceutical composition, wherein the composition comprises a therapeutically-effective amount of a compound (or a pharmaceutically acceptable salt thereof) recited in claim 50.

77. A compound or a salt thereof, wherein:

the compound corresponds in structure to Formula 77-1:



X is selected from the group consisting of $-O-R^1$, $-NH-O-R^2$, $-NH-O-R^3$, and $-NR^4R^5$; and

R^1 is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl, aryl, and aryl- C_1 - C_6 -alkyl; and

R^2 is a selectively removable protecting group; and

R^3 is selected from the group consisting of hydrogen and $C(W)R^6$; and

W is selected from the group consisting of O and S; and

R^6 is selected from the group consisting of C_1 - C_6 -alkyl, aryl, heteroaryl- C_1 - C_6 -alkyl, C_3 - C_8 -cycloalkyl- C_1 - C_6 -alkyl, aryl- C_1 - C_6 -alkyl, heteroaryl, and amino- C_1 - C_6 -alkyl, wherein the amino- C_1 - C_6 -alkyl nitrogen optionally is substituted with:

up to two substituents independently selected from the group consisting of C₁-C₆-alkyl, aryl, aryl-C₁-C₆-alkyl, C₃-C₈-cycloalkyl-C₁-C₆-alkyl, aryl-C₁-C₆-alkoxycarbonyl, C₁-C₆-alkoxycarbonyl, and C₁-C₆-alkylcarbonyl, or

5 two substituents such that the amino-C₁-C₆-alkyl nitrogen and two substituents together form a 5- to 8-member heterocyclyl; and as to R⁴ and R⁵:

R⁴ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₁-C₆-alkoxy, amino-C₁-C₆-alkyl, hydroxy-C₁-C₆-alkyl, aryl, aryloxy, and
10 aryl-C₁-C₆-alkyl; and R⁵ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, amino-C₁-C₆-alkyl, hydroxy-C₁-C₆-alkyl, aryl, and aryl-C₁-C₆-alkyl, or

R⁴ and R⁵, together with the nitrogen atom to which they are both bonded, form a 5- to 8-member ring optionally comprising up to one additional
15 heteroatom selected from the group consisting of oxygen, nitrogen, and sulfur; and as to A² and A³:

A² and A³, together with the carbon to which they are both bonded, form heterocyclyl or carbocyclyl, wherein:

20 the heterocyclyl or carbocyclyl optionally is substituted with up to 3 independently selected R^x substituents, and

the heterocyclyl or carbocyclyl optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

25 the optional heterocyclyl or carbocyclyl is, in turn, optionally substituted with up to 3 independently selected R^x substituents, or

A² and A³ are independently selected from the group consisting of hydrogen, alkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl,

carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocyclyoxyalkyl,
carbocyclylalkoxyalkyl, carbocyclylalkylthio, carbocyclylthioalkyl,
carbocyclylalkylthioalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl,
heterocyclylalkynyl, heterocyclyoxyalkyl, heterocyclylalkoxyalkyl,
5 heterocyclylalkylthio, heterocyclylthioalkyl, and heterocyclylalkylthioalkyl,
wherein:

any member of such group optionally is substituted with up to 3
independently selected R^x substituents, and

any member of such group optionally is substituted with two
10 substituents such that the two substituents, together with the atom(s) to
which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn,
optionally substituted with up to 3 independently selected R^x
substituents; and

15 E¹ is heteroaryl, wherein the heteroaryl optionally substituted with one or more
independently selected R^x substituents; and

Y is selected from the group consisting of halogen, nitro, azido,
phenylsulfoxido, aryloxy, C₂-C₆-alkoxy, C₁-C₆-alkylsulfonate, arylsulfonate, and
trisubstituted ammonium, wherein:

20 the trisubstituted ammonium substituents are independently selected
from the group consisting of aryl, aryl-C₁-C₆-alkyl, and C₁-C₆-alkyl; and
each R^x is independently selected from the group consisting of halogen, cyano,
hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy,
R^b-oxyalkyl, alkenyloxy, alkynyloxy, alkylthio, R^bR^b-amino, R^bR^b-aminoalkyl,
25 R^bR^b-aminoalkoxy, R^bR^b-aminoalkyl(R^b)amino, carbocyclyl, carbocyclylalkyl,
carbocyclyoxy, carbocyclyoxyalkoxy, carbocyclylthio, heterocyclyl,
heterocyclylalkyl, heterocyclyoxy, heterocyclyoxyalkoxy, heterocyclylthio,
alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl,
alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclylalkoxyalkyl,
30 carbocyclyliminocarbonyl, carbocyclylthioalkyl, carbocyclylsulfoxidoalkyl,
carbocyclylsulfonylalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkenyl,

carbocyclisulfonylalkenyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclisulfoxidoalkyl, heterocyclisulfonylalkyl, heterocyclylthioalkenyl, heterocyclisulfoxidoalkenyl, heterocyclisulfonylalkenyl, heterocyclyliminocarbonyl, aminosulfonylalkyl, and $-R^{x1}-R^{x2}$, wherein:

5 any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

 any member of such group optionally is substituted with one or
10 more substituents independently selected from the group consisting of halogen, hydroxy, and alkyl; and

 each R^{x1} is selected from the group consisting of $-C(O)-$, $-C(S)-$, $-C(NR^y)-$, $-S(O)-$, and $-S(O)_2-$; and

 each R^y is selected from the group consisting of hydrogen and hydroxy; and

15 each R^{x2} is selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy, R^b -oxyalkyl, alkenyloxy, alkynyloxy, R^bR^b -amino, R^bR^b -aminoalkyl, R^bR^b -aminoalkoxy, R^bR^b -aminoalkyl(R^b)amino, carbocyclyl, carbocyclylalkyl, carbocycloxy, carbocycloxyalkoxy, heterocyclyl, heterocyclylalkyl, heterocycloxy, and
20 heterocycloxyalkoxy, wherein:

 any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

25 any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy; and

 each R^b is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl, alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl, carbocyclylalkyl, carbocycloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl,
30

carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl,
carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocyclyoxyalkyl,
heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl,
heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl,

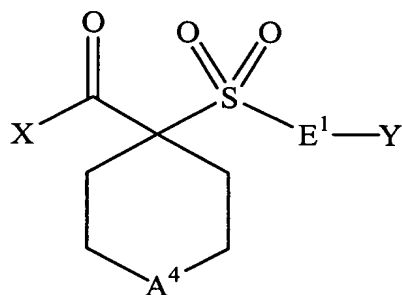
5 aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

any member of such group optionally is substituted with one or more
substituents independently selected from the group consisting of halogen,
hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl,
alkylcarbonyl, carbocyclyl, and carbocyclylalkyl.

10

78. A compound or salt thereof according to claim 77, wherein:

the compound corresponds in structure to Formula (78-1):



(78-1); and

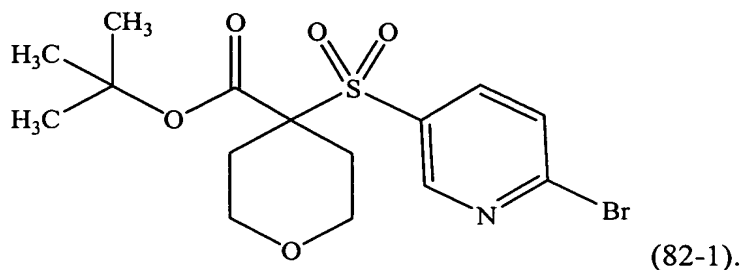
A⁴ is selected from the group consisting of -C(H)₂-, -C(R^x)(H)-, -C(R^x)₂-, -O-,
15 -N(H)-, -N(R^x)-, -S-, -S(O)-, and -S(O)₂-.

79. A compound or salt thereof according to claim 78, wherein Y is bromo.

80. A compound or salt thereof according to claim 78, wherein X is -NH-O-R²,
20 and R² is 2-tetrahydropyranyl.

81. A compound or salt thereof according to claim 78, wherein X is -O-R¹, and
R¹ is selected from the group consisting of hydrogen and t-butyl.

82. A compound or salt thereof according to claim 81, wherein the compound corresponds in structure to Formula (82-1):



- 5 83. A compound or salt thereof according to claim 78, wherein E¹ is selected from the group consisting of furanyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiodiazolyl, oxadiazolyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, oxathiazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, oxathiazinyl, oxepinyl, thiepinyl, benzofuranyl, isobenzofuranyl, benzoxazolyl, 10 benzoisoxazolyl, anthranilyl, benzothienyl, isobenzothienyl, benzothiazolyl, benzoisothiazolyl, benzothiadiazolyl, indoliziny, pyranopyrrolyl, benzoxadiazolyl, indolyl, isoindazolyl, benzoimidazolyl, benzotriazolyl, purinyl, imidazopyrazinyl, imidazolopyridazyl, quinolinyl, isoquinolinyl, pyridopyridinyl, phthalazinyl, quinoxalinyl, benzodiazinyl, pteridinyl, pyridazinotetrazinyl, pyrazinotetrazinyl, 15 pyrimidinotetrazinyl, benzoimidazothiazolyl, carbazolyl, and acridinyl, wherein:
any member of such group is substituted with one or more
independently selected R^x substituents.